PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

Schedule 5

SPRAVATO® Nasal Spray

contains 28 mg esketamine as hydrochloride

Read all of this leaflet carefully before you are given SPRAVATO

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse or other health care provider
- SPRAVATO has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What SPRAVATO is and what it is used for

What SPRAVATO is

SPRAVATO contains the active substance esketamine. This belongs to a group of medicines called anti-depressants and you have been given this medicine to treat your depression.

What SPRAVATO is used for

SPRAVATO is a nasal spray used in adults to reduce the symptoms of depression, such as, feeling sad, anxious (inner tension), or worthless, sleeping difficulties, change in appetite, difficulty in concentrating, loss of interest in favourite activities, feeling of being slowed down.

This medicine can help improve the symptoms of your disease and reduce the chance of your symptoms coming back.

SPRAVATO is used in people who have tried other anti-depressant medicines but have not benefited from them.

2. What you need to know before you use SPRAVATO

Do not use SPRAVATO if:

- you are hypersensitive (allergic) to esketamine, a similar medicine called ketamine used for anaesthesia, or any of the other ingredients of this medicine (listed in section 6).
- you have ever had certain conditions such as:
  - an “aneurysm” (this is a weak spot in a blood vessel wall where it widens or bulges out)

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- bleeding in the brain
- you recently had a heart attack (within 6 weeks)

This is because SPRAVATO can cause a temporary increase in blood pressure, that may lead to serious complications such as acute heart failure.

Do not use SPRAVATO if any of the above apply to you. If you are not sure, talk to your doctor before using SPRAVATO - your doctor will decide whether or not you can use this medicine.

Warnings and precautions

Talk to your doctor before using SPRAVATO if:

- you have heart problems which are not well controlled such as: poor blood flow in the blood vessels of the heart frequently with chest pain (such as “angina pectoris”), high blood pressure, a recent heart attack, heart valve disease or heart failure.
- you have ever had problems with the blood supply to your brain (such as “stroke”).
- you have ever had problems with drug abuse – prescribed or illegal drugs - or a problem with alcohol.
- you have ever had a condition called “psychosis” - where you believe in things that are not true (“delusions”) or see, feel, or hear things that are not there (“hallucinations”).
- you have ever had a condition called “bipolar disorder” or symptoms of mania (where you are very over-active or over-excited).
- you have ever had an overactive thyroid that is not properly treated (“hyperthyroidism”).

- you have ever had lung problems causing breathing difficulty ("pulmonary insufficiency", including chronic obstructive pulmonary disease [COPD]).
- you have ever had slow or fast heartbeats causing shortness of breath, palpitations or chest discomfort, feeling light-headed or fainting.
- you have had a serious head injury or serious problems affecting the brain, particularly where there is increased pressure in the brain.
- you have severe liver problems.

If any of the above apply to you (or you are not sure), talk to your doctor before using SPRAVATO. Your doctor will decide whether you should use this medicine.

Depression getting worse:

Tell your doctor or go to the nearest hospital straight away if you get the below while taking SPRAVATO:

- if you have thoughts of harming or killing yourself at any time. You may find it helpful to talk to a relative or close friend if you are depressed and ask them if they think your depression is getting worse or if they are worried about your behaviour. You might ask them to read this leaflet.

Blood pressure:

SPRAVATO can increase your blood pressure for a short time (about 1 to 2 hours) after you start to take it - so your blood pressure will be measured at various times. Your blood pressure will be measured before you start using SPRAVATO and after taking it.

If your blood pressure is high before using this medicine, your doctor will decide whether to start the medicine or wait until your blood pressure is lower. If your blood

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pressure increases significantly after using this medicine and remains elevated for more than a few hours after taking SPRAVATO, your doctor may send you to another doctor for evaluation.

This medicine may cause a temporary increase in your blood pressure after taking a dose. Your blood pressure will be checked before and after taking this medicine. Tell the medical staff right away if you get chest pain, shortness of breath, sudden severe headache, change in vision, or seizures after taking this medicine.

Tell your doctor if you get any of the below while you are taking SPRAVATO:

- difficulty with your attention, judgment and thinking (*See also "Driving and using machines" and "Possible side effects*"). During and after each use of this medicine, you will be checked by your doctor who will decide how long to monitor you. After being treated with this medicine, do not drive or use other machines that require you to be completely alert until the next day following a restful sleep.
- sleepiness (sedation), fainting, dizziness, spinning sensation, anxiety, or feeling disconnected from yourself, your thoughts, feelings, space and time (dissociation). Tell the medical staff right away if your feel like you cannot stay awake or if you feel like you are going to pass out.
- pain when urinating or seeing blood in your urine – these could be signs of urinary bladder problems. These have been seen when using high doses of a similar medicine (called ketamine), over a long period of time.

Tell your doctor if you get any of the above while you are taking SPRAVATO.

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Children and adolescents

Use of SPRAVATO has not been studied in children and adolescents younger than 18 years of age with treatment resistant depression. Therefore, SPRAVATO should not be used in this age group.

Other medicines and SPRAVATO

Always tell your healthcare provider if you are taking, have recently taken or might take any other medicines. (This includes all complementary or traditional medicines)

Taking SPRAVATO with certain medicines may cause side effects. Especially tell your doctor if you take:

- Central Nervous System (CNS) depressants (for example, benzodiazepines, opioids, medicines or beverages containing alcohol)
- Psychostimulants such as those used for conditions such as narcolepsy or medicines for ADHD (for example, amphetamines, methylphenidate, modafanil, armodafinil)
- Medicines for depression or Parkinson's disease: Monoamine oxidase inhibitors (MAOIs) (for example, tranylcypromine, selegiline, phenelzine).

Nasal sprays: If you need steroid or decongestant medicines as a nasal spray, avoid using these medicines within 1 hour before your SPRAVATO treatment.

SPRAVATO with food and drink

Some patients taking SPRAVATO may experience nausea or vomiting. You should avoid eating within 2 hours before and drinking liquids within 30 minutes before using this medicine.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or health care provider for advice before taking this medicine

Contraception

If you are able to become pregnant you must use highly effective contraception during treatment - and up to 6 weeks after the end of treatment. Talk with your doctor about methods of contraception to use.

Pregnancy

Do not use SPRAVATO if you are pregnant. If you are pregnant, think you may be pregnant or are planning to have a baby, tell your doctor before using this medicine. Using SPRAVATO during pregnancy has not been studied and it is not known if SPRAVATO will harm your unborn baby.

If you become pregnant while being treated with SPRAVATO, talk to your doctor straight away – to decide whether to stop treatment and to learn about other options for treatment.

Breastfeeding

Do not use SPRAVATO if you are breastfeeding. Talk to your doctor before using SPRVATO if you are breastfeeding. Your doctor will discuss with you whether to stop breastfeeding or stop using this medicine. Your doctor will take into account the benefit of breastfeeding for your child, and the benefit of treatment for you.

Driving and using machines

SPRAVATO can make you feel sleepy, dizzy, and have other side effects that can temporarily affect your ability to drive motor vehicles or use other machines and do anything where you need to be completely alert. After being treated with this medicine, do not take part in these activities until the next day following a restful sleep.

3. How to use SPRAVATO

Do not share medicines prescribed for you with any other person.

Always take SPRAVATO exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

Your doctor will tell you how long your treatment with SPRAVATO will last. Do not stop treatment early because your symptoms may return. If you have the impression that the effect of SPRAVATO is too strong or too weak, tell your doctor or pharmacist.

SPRAVATO is used together with another anti-depressant.
You will use the SPRAVATO yourself - under the supervision of your doctor in the doctor's office or clinic.

Your doctor will show you how to use the nasal spray device.
One nasal spray device delivers two sprays (one spray per nostril).
Your doctor will tell you how long your treatment with SPRAVATO will last. Do not stop early treatment.

How much to take

Your doctor will decide if you need 1, 2 or 3 nasal spray devices and how often you should come to the doctor's office or clinic for the medicine.

- SPRAVATO is usually taken twice a week for the first 4 weeks
- After the first 4 weeks, SPRAVATO is usually taken once a week
- After this, SPRAVATO is usually taken either once a week or once every 2 weeks.

During and after each use of this medicine, you will be checked and your doctor will decide how long to monitor you.

If you are given more SPRAVATO than needed

Since a healthcare provider will administer SPRAVATO, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you receive too much SPRAVATO, you may be more likely to experience side effects (*see "Possible side effects").*

If you forget a SPRAVATO treatment session(s)

In case a treatment session is missed, schedule the next session when the next dosage session was scheduled to occur. If more than 2 treatment sessions have been missed, your doctor will discuss any adjustment of your dose or frequency of SPRAVATO.

If you stop using SPRAVATO

It is important you make sure you come in for your scheduled appointments, so that this medicine is effective for you.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

SPRAVATO can have side effects.

Not all side effects reported for SPRAVATO are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking SPRAVATO, please consult your doctor, pharmacist or other healthcare professional for advice.

Tell your doctor if you notice any of the following side effects.

Frequent side effects

- feeling disconnected from yourself, your thoughts, feelings and things around you
- feeling dizzy
- headache
- change in sense of taste
- feeling sleepy
- decreased feeling or sensitivity, including around the mouth area
- spinning sensation (“vertigo”)
- vomiting
- nausea
- feeling extremely happy (“euphoria”)
- feeling agitated

- feeling anxious
- eyes, ears, or sense of touch are deceived or tricked in some way (something is not what it seems to be)
- feeling irritable
- panic attacks
- change in perception of time
- seeing, feeling, hearing or smelling things that are not there (hallucinations)
- feeling detached from reality
- problems with thinking
- muscle tremors
- feeling very sleepy with low energy
- difficulty speaking
- unusual feeling in the mouth (such as tingling or a crawling feeling)
- increased sensitivity to noise or sounds
- persistent ringing in the ears (tinnitus)
- blurred vision
- fast heartbeat
- nasal discomfort
- nasal dryness including dry crusts in the nose
- itchy nose
- dry mouth
- decreased feeling or sensitivity in the mouth
- excessive sweating
- frequent need to pass urine
- pain when passing urine
- urgent need to pass urine

- feeling abnormal
- feeling drunk
- feeling of body temperature change
- high blood pressure
- increased blood pressure

Less frequent side effects

- increased saliva

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: **https://www.sahpra.org.za/Publications/Index/8**. By reporting side effects, you can help provide more information on the safety of SPRAVATO.

5. How to store SPRAVATO

- Store all medicines out of the reach of children.
- Store at or below 30 ºC.
- Store in original package to protect from light and moisture.
- Do not use after the expiry date on the label/carton.

- Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage system (e.g., toilets).

6. Contents of the pack and other information

What SPRAVATO contains

The active substance is esketamine.

Each nasal spray device contains esketamine hydrochloride corresponding to 28 mg esketamine.

The other ingredients are:

Citric acid monohydrate

Disodium edetate

Sodium hydroxide (for pH adjustment)

Water for injections

What SPRAVATO looks like and contents of the pack

SPRAVATO is a nasal spray solution. This medicine is a clear, colourless solution, provided in a single-use nasal spray device.

SPRAVATO is available in pack sizes containing 1, 2, 3, or 6 nasal spray devices.

Each nasal spray device is individually packaged in a sealed blister.

Not all pack sizes may be marketed.

HOLDER OF CERTIFICATE OF REGISTRATION

JANSSEN PHARMACEUTICA (PTY) LTD

(Reg.No. 1980/011122/07)

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MedInfoZA@its.jnj.com

Registration/Application number

53/1.2/0732

Access to the corresponding Professional Information

Included in the carton, accompanying this patient information leaflet.